

Serial No. 10/576,038
Office Action mailed January 30, 2008
Amendment dated July 28, 2008
Docket No. 861-26-088-2

Amendment to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently Amended) A method of forming a polymer-biomacromolecule conjugate comprising radical based reaction of reacting a monomer with chemically active one or more user established polymerization initiation sites on a biomacromolecule, chemically active sites on the biomacromolecule or one or more user established sites on the biomacromolecule specifically modified by the user to include polymerization initiation sites, said method resulting in a polymer-biomacromolecule conjugate including a single biomolecule attached to one or more polymer chains.
2. (Currently Amended) The method of claim 1 wherein the chemically active one or more polymerization initiation sites or chemically active one or more sites on the biomacromolecule modified to include polymerization initiation sites comprise natural or non-natural amino acids.
3. (Original) The method of claim 2 wherein the biomacromolecule is a protein.
4. (Currently Amended) The method of claim 3 wherein the activated site is an amino acid is modified by an a protein modifying initiator or a protein modifying initiator is added to the protein to provide an initiator site, or an artificially created initiator amino acid is formed on the protein, or recombinant proteins are generated to include artificial amino acids containing an initiator fragment.
5. (Original) The method of claim 1 further including removing the unreacted monomer or non-bonded polymer to obtain a purified biomolecule-polymer conjugate.
6. (Currently Amended) The method of claim 4 wherein a non-interacting initiator which does not bind to the protein is added along with the protein modifying initiator and the polymer grown from non-interacting initiator is not covalently bound to the protein.
7. (Currently Amended) The method of claim 6 wherein a purified protein-polymer conjugate is obtained by further including removing any unreacted monomer or the non-

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covalently bound polymer grown from non-interacting initiator non-bonded polymer to obtain a purified protein polymer conjugate.

8. (Currently Amended) A method of forming a protein-polymer conjugate comprising modifying the protein to include initiator sites be reactive with a monomer and reacting the modified protein with said a monomer to form the protein-polymer conjugate comprising a single protein attached to one or more polymer chains.

9. (Currently Amended) A method of forming a protein-polymer conjugate comprising modifying the a protein to have one or more user established polymerization initiator sites functionality suitable for initiation of radical polymerization and reacting the modified protein with monomer to form a conjugate with the protein.

10. (Original) The method of claim 9 wherein the protein is modified to have bromoisobutyrate functionality and the conjugate is formed using atom transfer radical polymerization.

11. (Currently Amended) The method of claim 9 further including increasing the amount of reactive sites available to form user established polymerization sites by chemically creating in the protein reactive one or more free thiol sites available for conjugation of the initiator.

12. (Currently Amended) The method of claim 11 wherein the protein is reduced with tris-(2-carboxyethyl) phosphine hydrochloride to produce additional thiols on the protein for conjugation, modifying the protein by reacting with a pyridyl disulfide initiator conducted in the presence of a 2-bromoisobutyrate functionalized resin, capping any unmodified thiols with maleimide to form a macroinitiator and reacting the macroinitiator with a monomer with or without the presence of a 2-bromoisobutyrate functionalized resin to form the protein-polymer conjugate.

13. (Original) The method of claim 9 wherein the monomer and protein are reacted to form a conjugate including poly(N-isopropylacrylamide) or poly(ethylene glycol) methyl ether methacrylate.

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14. (Original) The method of claim 9 comprising modifying the protein by reacting it with propylmercapto-pyridine 2-bromoisobutyrate and then forming a conjugate by reacting with N-isopropylacrylamide.

15. (Currently Amended) A method of forming a protein-polymer conjugate comprising modifying a protein to have functionality suitable for initiation of radical polymerization and reacting the modified protein with a monomer The method of claim 9 comprising:

modifying the protein by interacting with a bromoisobutyrate-modified ligand initiator, mixing said protein modified by the bromoisobutyrate-modified ligand initiator with a non-interacting bromoisobutyrate-modified solid phase resin and adding to said mixture a suitable reactive monomer under conditions suitable to initiate polymerization of the protein modified by the bromoisobutyrate-modified ligand initiator with the monomer to form the protein-polymer conjugate.

16. (Original) The method of claim 15 wherein the initiator is a bromoisobutyrate-modified biotin initiator.

17. (Original) The method of claim 15 wherein the protein is streptavidin.

18. (Original) The method of claim 15 wherein the monomer is N-isopropylacrylamide.

19. (Original) The method of claim 15 wherein the monomer is (ethylene glycol) methyl ether methacrylate.

20. (Currently Amended) A protein-polymer conjugate comprising an a single initiator-modified protein bound to a one or more polymer chains with the initiator as a link between the single protein and the one or more polymer chains, the protein-polymer conjugate formed by reacting the initiator modified protein with a monomer and polymerizing to form the conjugate.

21. (Original) The method of claim 2 wherein the biomacromolecule is an enzyme.

22. (Original) The method of claim 21 wherein the enzyme is lysozyme.

23. (Original) The method of claim 2 wherein the biomacromolecule is an antibody.